DEVELOPMENT, CHARACTERIZATION AND EVALUATION OF FORMULATION BASED ON ACTIVE PHYTOCONSTITUENTS FOR DYSLIPIDEMIA AND OBESITY

A SYNOPSIS SUBMITTED FOR THE REGISTRATION OF DEGREE OF DOCTOR OF PHILOSOPHY

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Submitted

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ABSTRACT OF PROPOSED WORKPLAN:

The Present Synopsis is for the effect of herbal formulation on obese human subject is evaluated.

After proper literature survey the selected plant part will be collected and authenticate cleaned dried and powder of extraction with different solvent. Preliminary phytochemical investigation will be carried out. extract will be subjected for fractionation. The fractionated plant part extract will then evaluated for acute toxicity study for the determination of safe dose and screened for it anti-obesity effect .

INTRODUCTION

Obesity is a chronic and increasingly common health hazard characterized by excess body fat. It develops gradually and often persists throughout life. As a preventable cause of death in the US, obesity is second only to smoking. Traditionally, obesity was believed to be associated with affluent lifestyles in the west countries. However, obesity is a fast-growing problem in developing countries and is now known to be associated with increased health risks. Several studies in India have shown that changes in dietary patterns, physical activity levels, life styles associated with affluence and migration to urban areas are related to increasing risk of metabolic diseases such as type 2 diabetes mellitus, hypertension and dyslipidemia.

The most widely used method to gauge obesity is the Body mass index (BMI) and it focus in obesity treatment recommendations, with different treatment cutoff points based up on the presence or absence of obesity-related comorbid disease. In addition, many patients with these metabolic diseases are either overweight or obese. Important relationship between BMI and metabolic disease is critical toward a better understanding of the underlying pathophysiological processes leading to excessive fat-related metabolic disease. This study brings out the important risk factors for cardiovascular disease like hypertension and dyslipidemia in obese patients correlated with various BMI levels (**Dr.N.SURESH. March-2009).**

Excessive energy intake over energy expenditure gives rise to unwanted growth of adipose tissue leading to obesity. Because of its rising prevalent and its association with chronic health disorder such as insulin resistance, hyperlipidemia, hypertension, cardiovascular disease, non-alcoholic fatty liver and osteoarthritis. Obesity has turned out to be a major public health concern in both developed and developing countries. Conventional drug therapies of obesity are often assocated with adverse side effect and rebound weight gain when drug intake in discontinued (**Ramgopal mopuri et al 2015**). Control of excess body fat is one of the greatest health care challenges of our time.

Dyslipidemia is the imbalance of lipides such as cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides and high density lipoprotein (HDL).This condition can result from diet, tobacco exposure or genetic and it can lead to cardiovascular disease with server complication. sign and symptoms of dyslipidemia observed, chest pain or tightness, dizziness, heart palpitation, exhaustion, swelling of the ankles and feet, cold sweat, nausea and heart burnsJelena (**Vekic et al -2019).**

At 75th world health assembly in 2022 member of states adopted new recommendation for the prevention and management of obesity and endorsed the WHO acceleration plan to stop obesity. Obesity, in children, adolescent and adults is a public health concern in almost all regions of the world. As of 2016, it was estimated that 5.6% of adolescents aged 10-19 years were obese higher than 2 standard deviation from the WHO reference 2007 in order to respond to current global epidemiology and to complement existing prevention-focused guideline, the world health organization (WHO)(www.google **publication 3 july 2023).**

Review of literature:

Previous work done in relevant area literature shows:

Karale et al: momordica charantia L is possessed various beneficial effects, including anti-inflammatory, antioxidant, cytotoxic, anticancer, anti-obesity, antiviral, anti-HIV, antiulcer cholesterol lowering, inhibition of protein tyrosine phosphatase and antiosteoporosis[5]. Terminalia paniculata Roth (family- Combretaceae) is tropical tree in western and southern parts of India. In the present study, in addition of LC-MS/MS analysis of TPEE on body weight, total fat, fat free mass, fat%, serum lipid profiles and the levels of leptin adiponectin, insulin and liver marker enzymes.

Prakash Raj Pandeya et al: have reported anti-adipogenic activity of herbal formulation F2 in 3T3-L1 adipocytes in vitro and preliminary anti-obesity activity in HED-fed C57BL/6J mice in vivo. F2 was prepared by mixing specific proportions of a trace amount of royal jelly and lemon juice with ethanol of Orostachys japonica(OJ), Rhus verniciflua(RV) and Geranium thunbergia (GT).In the observation of that F2 formulation ingredient synergistically inhibited adipose differentiation, restricted dietary fat absorption and reduced fat accumulation in the tissue[8].

Blocking nutrient absorption is one of the therapeutic strategies to reduce energy intake and thereby bogy weight pancreatic lipase, a key enzyme involved in dietary fat absorption is considered to be a viable anti-obesity drug target and its inhibition[9].

The literature shows the hypocholesterolemic effect of Allium cepa L., Allium sativum L., Glycine max (L.), Trigonella foenum-graecum L., Moringa oleifera Lam., Sesamum indicum L., Luffa species and variety of plants from Cucurbitaceae family have traditional claims and reported potent antihyperlipidemic potential. Onion contains many sulphur containing active principles, which takes part in biological activities, mainly in the form of cysteine derivatives, namely, S-alkyl cysteine sulfoxides that decompose into a variety of thiosulfinates and polysulfides by the action of an enzyme allinase on extraction[16].

Timo D.Muller, Mattias bluher, Matthias h. Tschop and Richard D.Dimarchi, anti-obesity drug discovery advances and challenges - the treatment of obesity itself has proven largely resistance to therapy, with anti-obesity medication (AOM)[6]. Cyclocarya paliurus batal -native china is widely consumed as a chinese traditional folk medicines for the prevention and treatment of hyperlipidemic obesity and diabetes. Result- different cyclocarya paliurus polar extract especially ChE reduced the levels of serum, total cholesterol (TC), triglycerides (TG), Low density lipoprotein cholesterol (LDL-C)[7].

The traditional Indian medicinal plants derived products have been reported to be effective for treating various metabolic and systemic disorders. By employing the in-vitro cell based adipogenesis model as a screening tool, we selected Moringa oleifera, Murraya koenigii and Curcuma longa extracts, which exhibited adipogenesis inhibition potential[3].

Moringa oleifera is commonly known as the “drumstick” tree. This plant has medicinal importance and is being used in folk medicine for treatment of variety of human ailments such as rheumatism, paralysis and epilepsy. It also has great value as a food ingredient. The leaves, pods, seeds, flowers, and roots of the M. oleifera tree are edible and nontoxic[3].

Murraya koenigii is commonly known as curry leaf. This plant is native to India and is widely available throughout the Indian subcontinent excluding the high altitudes of the Himalayas. Curry leaf is used in folk medicine in India and in other asian countries as analgesic, astringent, anti-dysenteric, febrifuge, hypolipidemic and hypoglycemic agent[13].

Eurycoma Longifolia and Brucea Javanica (Both from family Simaroubaceae) were investigated for their lipolytic activity, a bioactivity to break down triglyceride into glycerol in adipocytes. Several lipolytic compounds were isolated from these plants[17].

Turmeric (Curcuma longa) has a long tradition of being used as a common spice in the Indian subcontinent and by many cultures across the globe. In Chinese and ayurvedic systems of medicine, it has been described as an anti-inflammatory agent, and used for the treatment of jaundice, menstrual disturbances, hematuria, hemorrhage, and colic etc. It also possesses potent anti-oxidant ability. Turmeric extracts are also used as hepatoprotective, nephroprotective, anti-asthmatic, anti-tumor agents and as a detoxifier and regenerator of liver tissue etc. Curcumins are the group of active compounds in turmeric.

Many Siddha medicinal plants showed anti-obesity activities that can be utilized in the management of obesity, through which the complications of obesity can be prevented. Most researches explored the anti-obesity potentials of medicinal plants. Terminalia chebula, Phyllanthus niruri, zingiber officinale, Piper longum, Curcuma longa, Elettaria cardamomum, Cuminum cyminum, Picrorhiza kurroa, Ipomea turpethum, Tinospora cordifolia, Michelia champaka are some medicinal plants possess anti-obesity properties that had been indicated in Siddha[1].

NEED OF THE PRESENT INVESTIGATION:

Now day obesity affecting all age groups of both sexes. now one third of world population is overweight or obese.so the treatment is based on current issue of world investigation need.

A literature survey show that various polyherbal formulation on antiobesity are available in market but formulation based on balancing of all tridosa and controlling obesity are rare.In this research I am minimizing the disadvantages of previous literature to get optimizing formulation to desired therapeutic effect.in that the targeted based study will do so that doesn’t do any researcher.

Blocking nutrient absorption is one of the therapeutic strategies to reduce energy intake and there by body weight. Pancreatic lipase, a key enzyme involved in dietary fat absorption, is considered to be a viable anti-obesity drug target and its inhibition leads to the reduction of dietary fat absorption, energy intake, and has implications in weight reduction.

OBJECTIVE OF RESEARCH:

Literature survey reveals that several plants have been proven better source of drug. Using the medicinal source of the drug to develop formulation from herbal product is

- To select active phytoconstituent on the basis of literature
- To insilico characterization of selected phytoconstituents.
- To design and development of suitable dosage form.
- To optimization and characterization of dosage forms.
- To evaluation of anti-obesity and anti-dyslipidemic potential of optimized formulation.
- The primary objective is to determine the efficacy of natural formulation in reducing body weight, BMI and normalizing lipid profile.
- To investigate the anti-obesity or antihyperlipidemic activity of plant extract.
- This research study explore the potential therapeutic role of Herbal formulation.
- This study was design to investigate anti-obesity activity of herbal formulation on high fat diet obese patient.
- To disseminate of the research finding by publication for the health care provider and lay public.

RESEARCH METHODOLOGY:

I. Literature review: Literature survey will be carried out by referring the books, related journals. By using internet access, various national as well as international journals will be followed for reference.

II. Selection of plant constituents on the basis of literature, in-silico characterization, screening of phytoconstituent for antidyslipidemic and antiobesity potential by in-vitro and in-vivo method.

III. Formulation Development:

- Development of Polyherbal formulation will base on balancing of all tridosha.
- Selection of right combination of the active ingredients in the Polyherbal formulation.
- Determination of concentration ranges of each active ingredients.
- Determination of dosage form of the formulation.
- Determination of proposed dose of the formulation.
- Time range selection of each kind of formulation.

IV. Preclinical study:

Evaluation of optimized formulation for antidyslipidemic and antiobesity potential by in-vivo method .

Animal Study plan:

- Procurement of animals for the required study
- Route of administration for the study
- Effectiveness of the anti-obesity and antidyslipidemic polyherbal formulation on animals
- Prediction of mode action of the drugs

METHODOLOGY TO BE ADOPTED:

IMPORTANT OF STUDY:

INTERNATIONAL STATUS: Obesity is the biggest issue in a current generation disorder. Currently in the world 38% of population is overweight. The world obesity federation report in 2023 stated that in the recent upcoming year, the number of people of obesity will increase. Almost half of the population will be affected by the obesity. The international report said that in the upcoming 12 years, 4 billion people will be suffering from obesity and most of them will be children of young age.

NATIONAL STATUS:

Obesity in India has reached epidemic proportions in the 21st century with morbid obesity affecting 5% of the country's population. As per the NFHS-5 data 23% of women and 22.1% of men are overweight as per the BMI criterion. The preliminary finding on the status of abdominal obesity reveals that 40% of women and 12% of men are abdominal obese in the country.

SCOPE OF STUDY:-

The study will be supportive to treat the various complication due to hyper lipidemia and obesity in patients. Herbal formulation medicine expected to have fewer side effect as compared to the modern allopathic drugs The present study will be helpful community minimize the cost of the treatment of disease due to hyper lipidemia. This study uses the various plant extract as a medicine which have been not fully explored and clinical trial not yet done on it that's why it will very important to investigate the anti-hyperlipidemic clinical trial. This study of functional to get prior component using this to get maximum therapeutic result of Herbal product the study anticipated benefit for the individual trail subject and society.

PROPOSED WORKS PLAN:

First Year:

- ❖ Collection of plant material, identification of plants.
- ➢ Preparation of extracts by using various solvents, procurement, drying of extracts
- ➢ Phytochemical screening of extracts
- ➢ Toxicity evaluation, preliminary studies and main studies.

Second year:

- ➢ Fractionation of potent extract
- ➢ Antihyperlipidemic activity of selected fractions
- ➢ Separation and isolation of compound by TLC, HPTLC, column chromatography

Third year:

- ➢ Preparation of polyherbal formulation
- ➢ Evaluation of antihyperlipidemic potential of selected polyherbal formulation and comparison with standard marketed products.

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